

Claims

[1] 1. A process for preparing 1,8-naphthyridine-3-carboxylic acid derivative comprising:

[2] the first step a) the compound of the following formula (1),

[3]

(1)

is reacted with dimethylformamide dialkylacetal of formula $\text{Me}_2\text{NCH}(\text{OR})_2$ (wherein R represents straight-chain, branched or cyclic alkyl having 1 to 9 carbon atoms, or represents benzyl) in a solvent in the presence of acid catalyst to prepare the compound of the following formula (2),

[4]

(2)

the second step b) the resulting reaction mixture of the following formula (2),

[6]

(2)

[7] is reacted with amine of formula YHNH_2 to prepare the compound of the following formula (3),

[8]

(3)

in which

Y represents straight-chain, branched or cyclic alkyl, having 1 to 5 carbon atoms, and unsubstituted or substituted by halogen, or represents phenyl unsubstituted or substituted by halogen,

[9]

[10] the third step c) the resulting compound of the following formula (3),

[11]

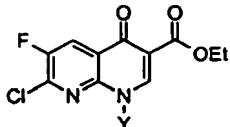
(3)

in which

Y is as defined above,

[12] is cyclized in the presence of quaternary ammonium salt and a base to prepare 1,8-naphthyridine-3-carboxylic acid ester of the following formula (4),

[13]



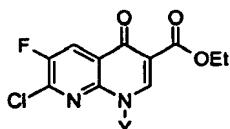
(4)

in which

Y is as defined above, and

in the fourth step d) the resulting compound of the following formula (4),

[14]



(4)

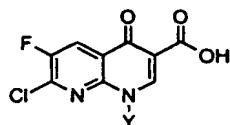
in which

Y is as defined above,

is hydrolyzed in the presence of an acid to prepare

1,8-naphthyridine-3-carboxylic acid derivative of the following formula (5),

[15]



[16]

(5)

[17]

in which

Y is as defined above,

is characterized by one pot operation of the above steps using single solvent system without intermediate isolation.

[18]

2. The process according to claim 1 wherein R represents methyl.

[19]

3. The process according to claim 1 wherein the solvent used is toluene.

[20]

4. The process according to claim 1 wherein dimethylformamide dialkylacetal of formula $\text{[Me}_2\text{NCH(OR)}_2]$ is employed from 1.05 to 1.15 mole equivalents per mole of the compound of formula (1)

[21]

5. The process according to claim 1 wherein in the step a), acetic acid as acid catalyst is employed from 0.2 to 0.3 mole equivalents per mole of the compound

of formula (1)

- [22] 6. The process according to claim 1 wherein amine of formula $\text{Y}(\text{NH}_2)_2$ is cyclopropylamine.
- [23] 7. The process according to claim 1 wherein amine of formula $\text{Y}(\text{NH}_2)_2$ is employed from 1.1 to 1.2 mole equivalents per mole of the compound of formula (1).
- [24] 8. The process according to claim 1 wherein the reaction solution after the step b) is washed with aqueous citric acid solution.
- [25] 9. The process according to claim 1 wherein in the step c), aqueous tetrabutylammonium hydroxide solution is used as base.
- [26] 10. The process according to claim 1 wherein in the step d), the reaction solution is heated under reflux by using concentrated aqueous hydrochloric acid.